

REMARKS

Claims 1 and 9-23 are pending. Claims 11, 14 and 19-23 are withdrawn. Claims 2-8 were previously cancelled. Claims 1, 15-17 and 23 have been amended. Specifically, claims 1 and 23 have been amended to further specify the claimed invention. Support for the amendments to claims 1 and 23 can be found in the specification as filed, at least at page 4, line 13; page 7, formula (Id); and page 2, lines 12-15. Claim 15 has been amended to further specify the claimed invention. Support for the amendments to claim 15 can be found in the specification as filed, at least at pages 31-61. Claim 16 has been amended to correct a minor typographical error. Claim 17 has been amended to be in independent format.

No new matter has been added.

The Examiner objects to claims 16 and 17 for depending on a rejected base claim. Claim 16 properly depend from amended claim 1, which Applicant submits is allowable. Claim 17 has been amended to be in independent format. Therefore, objection with respect to claims 16 and 17 is respectfully requested.

Claim Rejections—35 USC § 112

The Examiner states that claim 15 is rejected under 35 USC § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Examiner states that claim 15 does not define the invention because claims that incorporate by reference the exemplified compounds in the specification are not specific. Claim 15 has been amended to recite the chemical names of the exemplified compounds. As such, claim 15 is definite. Withdrawal of the rejection is respectfully requested.

The Examiner states that claims 1, 9, 12-13 and 18 are rejected under 35 USC § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicants regard as the invention. The Examiner alleges that the definition of variable R² from claim 1 lacks clarity:

“R² is 4- to 7-membered cycloalkyl substituted by R³, C(O)OR³, C(O)R³ or S(O)₂R³, or 4- to 7-membered heterocyclyl, containing one or two nitrogen atoms which is unsubstituted or substituted by C(O)OR⁴, C(O)R³, S(O)₂R³, C(O)NHR⁴, P(O)(OR¹¹)₂ or a 5- or 6-membered nitrogen containing heteroaryl group;”

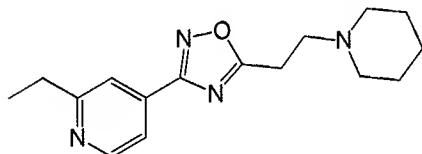
Specifically, the Examiner alleges that it is unclear whether “a 5- or 6-membered nitrogen containing heteroaryl group” is an option for variable R², or whether it is a substituent when R² is substituted 4- to 7- membered heterocycle. Applicants have amended the variable R² from claim 1 as follows:

“R² is 4- to 7-membered cycloalkyl substituted by R³, C(O)OR³, C(O)R³ or S(O)₂R³, or R² is 4- to 7-membered heterocycl¹, wherein the heterocycle contains one nitrogen atom which is substituted by ~~e~~containing one or two nitrogen atoms which is unsubstituted or substituted by C(O)OR⁴, C(O)R³, S(O)₂R³, C(O)NHR⁴, P(O)(OR¹¹)₂ or a 5- or 6-membered nitrogen containing heteroaryl group;”

As such, claim 1 (and claims that depend directly or indirectly therefrom) is definite and sufficiently clear. Withdrawal of the rejection is respectfully requested.

Claim Rejections—35 USC § 102

The Examiner states that claims 1, 9, and 18 are rejected under 35 USC § 102(b) as being anticipated by US Patent No. 3,647,809 (hereinafter referred to as Reiter). Specifically, the Examiner notes that Reiter teaches the compound where B is –CH₂-CH₂, wherein n is 2, R² is 6 membered heterocycl¹ containing one nitrogen atom, Y is O, X is N, and R¹ is 4-pyridyl substituted with ethyl, which is construed to be:

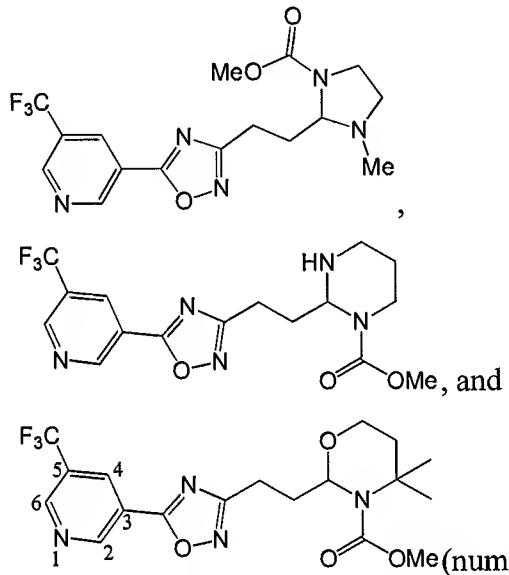


. Applicants respectfully disagree in view of the claim amendments.

Claim 1 has been amended to recite R² can be a 6 membered heterocycl¹, “wherein the heterocycl¹ contains one nitrogen atom which is substituted by C(O)OR⁴, C(O)R³, S(O)₂R³, C(O)NHR⁴, P(O)(OR¹¹)₂ or a 5- or 6-membered nitrogen containing heteroaryl group”. Thus, the amended claims recite compounds containing a heterocycle with a nitrogen substituted by the claimed groups stated above. Reiter does not recite each and every aspect of the claimed invention and cannot anticipate the claims. Therefore, withdrawal of the rejection is respectfully requested.

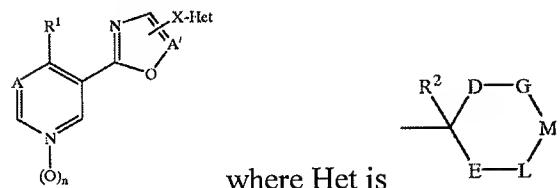
Claim Rejections—35 USC § 103

The Examiner states that claims 1, 9, 10, 12, 13 and 18 are rejected under 35 USC § 103(a) as being unpatentable over WO 2002/012229 (which corresponds to US 2002/0132813; hereinafter referred to as Schaper). The Examiner cites the following compounds taught by Schaper:



connected at the 3-position rather than the instantly claimed 4-position. The Examiner alleges that one of ordinary skill would be motivated, from the disclosure in Schaper, to make the modifications required to arrive at the instant invention with reasonable expectation of success for obtaining a compound with the same utility. Applicants respectfully traverse.

Schaper teaches compounds for the use of controlling animal pests having formula (I):

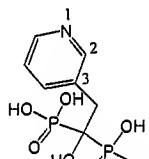


(O)_n where Het is $\begin{array}{c} \text{E} \\ \diagdown \\ \text{L} \end{array}$. The compounds taught by Schaper are completely different from the claimed compounds. Specifically, both variables D and E in Schaper are heteroatoms whereas the claimed compounds contain only one heteroatom. In other words, when R² of the claimed compounds is a heterocycle, the heterocycle contains only one nitrogen atom, whereas Schaper teaches compounds containing a heterocycle with at least two heteroatoms.

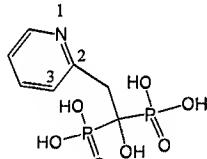
Replacing a carbon atom with a heteroatom (e.g., nitrogen) could significantly affect the electron density of the resultant heterocyclic ring, resulting in significant differences in the molecule's interaction with the receptor, its function, bioavailability, and/or metabolism.

Further, Schaper even teaches that the "most preferred compounds" are those where both "D and E are oxygen", i.e., not nitrogen. See page 2, paragraphs [0053] and [0057] and page 10, paragraph [0138] of Schaper. A skilled artisan would not be motivated to select the nitrogen-substituted heterocycle compounds from Schaper for further modification as Schaper teaches that the preferred compounds are oxygen substituted heterocycle compounds. Thus, a skilled artisan reading Schaper would not be motivated to modify the heterocycle to contain only one heteroatom, let alone to a heterocycle containing one (substituted) nitrogen atom.

Regarding the Examiner's allegation that Schaper's compounds are positional isomers of the claimed compounds which would motivate a skilled artisan to arrive at the instant invention, Applicants respectfully direct the Examiner to *Procter & Gamble Co. v. Teva Pharmaceuticals USA, Inc.*, 566 F.3d 989 (Fed. Cir. 2009), where the Court held that the claims covering



risedronate: are not obvious in view of prior art that disclosed the positional isomer



2-pyr EHDHP: *Id.* at 995. The hydroxyl-ethane-diphosphonate group is connected to the #3 carbon of a pyridine ring in the claimed compounds, while in the prior art, 2-pyr EHDHP, the hydroxyl-ethane-diphosphonate group is connected to the #2 carbon. *Id.* The Court reasoned that because the nitrogen atom is in a different position in the two molecules, they differ in three dimensional shape, charge distribution and hydrogen bonding properties, and are therefore not obvious variants. *Id.*

The compounds of claim 1 are substituted at the 4-position with respect to the nitrogen in the pyridine ring rather than at the 3-position as disclosed in the cited compounds from Schaper.

In view of the teachings of *Proctor & Gamble*, the claimed compounds are not obvious based on the Schaper's teachings.

Further, the Federal Circuit recently addressed obviousness of closely-related chemical structures in *Takeda Chem. Indus., Ltd. V. Alphapharm Pty., Ltd.*, 492 F.3d 1350 (Fed. Cir. 2007). Specifically, citing *In re Deuel*, 51 F.3d 1552, the Court stated, “A known compound may suggest its homolog, analog, or isomer because such compounds ‘often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties.’” The Court clarified however, “that in order to find a *prima facie* case of unpatentability in such cases, a showing that the ‘prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention’ was also required.”

The Court further held in Takeda, “[t]hus in cases involving new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish a *prima facie* obviousness of a new claimed compound.”

Still further, the CAFC has elucidated the obviousness factors for chemical structures in *Eisai v. Dr. Reddy's Laboratories*, 533 F.3d 1353 (Fed. Cir. 2008). The CAFC discussed the *Graham* factors in new chemical composition cases, stating, “Post-KSR, a *prima facie* case of obviousness for a chemical compound still, in general, begins with the reasoned identification of a lead compound.” It is therefore necessary that in order to establish a *prima facie* case of obviousness for a chemical composition of matter, it is necessary to establish a lead compound from the prior art. It is further necessary to establish a showing that the prior art would have suggested making the specific molecular modifications to the lead compound necessary in order to achieve the claimed invention.

In the present case, the Examiner has neither identified a “lead compound” nor identified a teaching in the art which would lead one of skill to make the modifications to arrive at the claimed invention. In the absence of such an analysis, a *prima facie* case of obviousness has not been established. An obviousness rejection of a chemical compound is improper without the reasoned identification of a lead compound.

While the Examiner describes three examples of compounds from Schaper, there is no

reason for selecting these particular compounds as a lead compounds. The Examiner has failed to point to any data from Schaper showing that these compounds possess superior properties relative to the other compounds described therein. There are many compounds described in Schaper. Schaper teaches that the preferred compounds have a heterocycle substituted with two oxygen atoms. Thus, without more, one of ordinary skill would not have selected these three compounds with a nitrogen-substituted heterocycle for further modification.

Even assuming *arguendo* that Schaper identifies the above cited compounds as lead compounds (Applicants assert Schaper does not), Schaper does not provide any reason to modify the cited compounds to arrive at the particular compounds claimed. Specifically, there is no reason to (1) select the specific oxadiazole substituent to attach at the 4-position of the pyridine ring from those exemplified by Schaper, or (2) replace D or E with a carbon atom in the heterocycle as Schaper does not describe any structural feature that is particularly important for the desired activity. Even if one did select the three cited compounds as lead compounds, there is no reason to modify any of them to arrive at the particular compounds claimed.

Schaper does not teach modifying the compounds to make the claimed compounds. At most, one would have to pick and choose, piece-meal, amongst features of the reference to try to attempt to arrive at the compounds of the present invention. Even if the skilled artisan were to start with any of the compounds of disclosed by Schaper and attempt to modify the teachings of Schaper to arrive at the compounds of present invention, it is submitted that the artisan would need to exercise thought and skill that in itself would require a level of inventive skill beyond that which could ordinarily expected. Therefore, the claimed compounds are not obvious based on Schaper's teachings.

Thus, the Examiner has failed to make a *prima facie* case of obviousness.

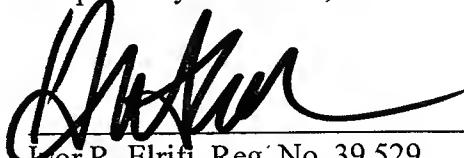
Applicants submit that as-amended the claims are not obvious in view of Schaper and requests withdrawal of the rejection.

APPLICANTS: Fyfe et al.
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CONCLUSION

On the basis of the foregoing amendments, Applicants respectfully submit that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,



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